Remarks

In view of the above amendments and the following remarks, reconsideration of the outstanding office action is respectfully requested.

Claims 1-3, 5-7, 9, and 10 have been amended and claim 4 has been canceled without prejudice. New claims 40-51 have been added. Descriptive support for claims 40, 45, and 46 is provided where noted in response to the various 'written description' rejections discussed below. Descriptive support for claims 41-44 appears in Examples 9 and 10. Descriptive support for claims 47-51 is provided in original claims 6-10. No new matter has been entered.

The rejection of claims 1-10 under 35 U.S.C. § 112 (first paragraph) for want of written descriptive support for the phrase "a DNA molecule from a source other than *Pseudomonas syringae* pv. *tomato*" is rendered moot by the above amendments.

To the extent the rejection applies to new claims 40-51, however, the rejection is respectfully traversed. The basis asserted by the U.S. Patent and Trademark Office ("PTO") for this rejection is contrary to law.

In this case, the specification identifies a species by nucleotide sequence (the *hrpW* sequence of SEQ ID NO: 1, which was isolated from *Pseudomonas syringae* pv. *tomato*), and the genus by the property of hybridization to SEQ ID NO: 1 or, more specifically, its complement. Because SEQ ID NO: 1 represents the *hrpW* species from *Pseudomonas syringae* pv. *tomato* and the remaining species encompassed by the genus will be from other pathogen (e.g., other *Pseudomonas syringae* pathovars, *Pseudomonas viridiflava*, *Ralstonia solanacearum*, and *Xanthomonas campestris*, eleven of which are identified in Examples 5 and 10), it is appropriate to consider the subject matter of SEQ ID NO: 1 excluded from the scope of claim 40.

Furthermore, the objected-to language was introduced for purposes of explicitly excluding from the scope of the hybridization language, originally presented as alternative (c) of claim 1 but now presented in claim 40, the nucleic acid identified by Lorang et al., *Mol. Plant-Microbe Interact.*, 8:49-57 (1995) ("Lorang"), which partially overlaps with the sequence of SEQ ID NO: 1. Contrary to the PTO's assertion at page 3 of the outstanding office action, the incorporation by reference of Lorang into the specification (see page 5, line 14; page 27, lines 8 and 23; page 31, line 12; and page 33, line 19) does allow applicant to exclude such subject matter from the scope of the genus of claim 40.

It is well established law that satisfaction of the written description requirement does not require *ipsis verbis* support in the specification. *See In re Wertheim*, 541 F.2d 257, 265, 191 USPQ 90, 98 (CCPA 1976) (citing *In re Lukach*, 442 F.2d 967, 969, 169 USPQ 795, 796 (CCPA 1971)). Instead, the specification need only demonstrate to one of ordinary skill in the art that applicants invented the claimed subject matter. *See In re Gostelli*, 872 F.2d 1008, 1012 (Fed. Cir. 1989); *Union Oil Co. v. Atlantic Richfield Co.*, 208 F.3d 989, 1001, 54 USPQ2d 1227, 1232 (Fed. Cir. 2000). As discussed above, the objected-to language effects an exclusion of a disclosed species from the disclosed genus. This is a perfectly legitimate procedure. *See In re Johnson*, 558 F.2d 1008, 1017-1018, 194 USPQ 187, 195 (CCPA 1977) (written descriptive support for a subgenus does exist where both the excluded species and the genus are disclosed). Of particular import in this instance is the fact that the CCPA, predecessor to the Federal Circuit, has criticized the PTO for hypertechnical application of the written description requirement as in the present case. *See id.* at 1019, 194 USPQ at 196. All that has happened in this application is that applicants have narrowed claim 40 to avoid having it read on a species identified in the prior art (e.g., the partial sequence disclosed in Lorang).

For all these reasons, the above-identified language finds written descriptive support in the specification and is not new matter. The rejection of claims 1-10 should therefore be withdrawn and should not be applied to new claims 40-51.

The rejection of claims 1-10 under 35 U.S.C. § 112 (first paragraph) as lacking written descriptive support for the phrase "wash conditions effective to remove DNA that binds non-specifically to the DNA molecule" is rendered moot and should be withdrawn.

The rejection of claims 1 and 4-10 under 35 U.S.C. § 112 (first paragraph) for lack of enablement is rendered moot with respect to claims 1 and 4-10, and is respectfully traversed with respect to new claims 40-51.

Claim 40 recites both hybridization and wash conditions as follows: "hybridization conditions comprising hybridization at 62°C for 8 hours in a hybridization medium that contains about 1.7M Na^+ followed by wash conditions comprising a wash medium that contains 1.0% SDS and 0.2X SSC." Moreover, claim 40 correlates structural homogeneity imposed by the hybridization conditions with protein function, reciting that the DNA molecule encodes "a polypeptide that elicits a hypersensitive response in non-host plants."

Given the recitation of the hybridization and wash conditions, one of ordinary skill in the art would have been able to carry out the hybridization procedure in August 1997.

It is well established law that matter which is known to those of ordinary skill in the art need not be included in the specification. *See Paperless Accounting, Inc. v. Bay Area Rapid Transit Sys.*, 804 F.2d 659, 664, 231 USPQ 649, 653 (Fed. Cir. 1986) ("A patent applicant need not include in the specification that which is already known to and available to the public."). In fact, a patent preferably omits that which is well known in the art. *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986).

The hybridization procedure described in Examples 5 and 10 is a standard one. The hybridization and wash conditions described for performing the procedure are disclosed in those examples. The hybridization probe was a radiolabeled *hrpW* probe (page 25, lines 1-3). It was well-known in August 1997 that the wash is preferably performed at various temperatures and various times (i.e., from 5 to 30 minutes at temperatures ranging from room temperature up to 68°C). *See* Sambrook et al., *Molecular Cloning: A Laboratory Manual*, (Cold Spring Harbor Laboratory, Cold Spring Harbor, NY) (1989) pp. 9.47-9.57 ("Sambrook") (copy attached as Exhibit 1) at 9.54. The wash is typically performed until no further radioactivity is detected in regions of the membrane that do not contain DNA. *Id.*

Moreover, given applicants' identification of a single species of *hrpW* by its nucleotide sequence (as well as the amino acid sequence of its encoded HrpW protein) and the demonstration that HrpW homologs exist in other Gram-negative pathogens (e.g., *Pseudomonas syringae* pathovars *glycinea*, *papulans*, *pisi*, *phaseolicola*, *tabaci*, and *syringae* strains B728a and 61, *Pseudomonas viridiflava*, *Ralstonia solanacearum*, and *Xanthomonas campestris* pathovars *amoraciae* and *vesicatoria*), one of ordinary skill in the art would have expected HrpW to be distributed widely among Gram negative pathogens. This fact is further evidenced by the post-filing date demonstration, by routine Southern hybridization, that HrpW is indeed widely dispersed among Gram negative pathogens (see Guttman et al., "A Functional Screen for the Type III (Hrp) Secretome of the Plant Pathogen *Pseudomonas syringae*," *Science* 295:1722-1726 (2002) ("Guttman") at Table 3)(reporting distribution of HrpW among *Pseudomonas syringae* pathovars *maculicola*, *phaseolicola*, *tomato*, and *syringae*, as well as *Pseudomonas* species *viridflava*, *chicorii*, *fluorescence*, *putida*, *stutzeri*, *aeruginosa*, and *Ralstonia solanacearum*, *Xanthomonas campestris* pv. *campestris*, and *Burkholderia capacia*) (copy attached to April 15, 2003, response as Exhibit B). The Southern procedure described by Guttman relies on the Southern protocol of Sambrook (*see* Guttman, Table 3 description and citation to reference '45'). The later work of Guttman therefore supports applicants' claim to the isolated DNA molecule of claim 40.

Contrary to the PTO's assertion that applicants did not sequence any of the recovered genomic DNA from other plant pathogens, applicants did do so. In particular,

applicants performed restriction mapping and partial DNA sequence analysis between the DC3000 *hrpW* and cosmid pCPP2347, which is derived from *P. syringae* pv. *syringae* B728a and carries DNA hybridizing with *hrpW* of DC3000. This restriction mapping and partial DNA sequence analysis indicated that the analyzed region is highly conserved in these two *P. syringae* pathovars and that the *P. syringae* pv. *syringae* B728a HrpW also carries a Pel domain (*see* Example 10 and Figure 2A). Thus, in addition to identifying the presence of eleven *hrpW* homologs from diverse plant pathogenic species, the applicants demonstrated that the results of the hybridization are predictive of a DNA molecule encoding a structurally similar HrpW polypeptide. Therefore, applicants did not need to identify any further *hrpW* homologs by their complete nucleotide sequence in order to enable others to obtain the same.

Applicants further submit that one of ordinary skill would have been fully able to express the protein from a recovered DNA molecule hybridizing to the complement of SEQ ID NO: 1 (see specification at page 11, line 7 to page 14, line 23, describing recombinant techniques and protein purification procedures) and then determine whether the encoded protein does in fact elicit a hypersensitive response when infiltrated onto non-host plants. As demonstrated in Example 11 of the present application, the protein preparation can be infiltrated onto tobacco leaves to assay whether a hypersensitive response-like necrosis is induced (see specification at page 29, lines 22 and Figure 5). To do so would require nothing more that routine experimentation.

For all these reasons, the rejection of claims 1 and 4-10 for lack of enablement should be withdrawn, and should not be applied to new claims 40-51.

The rejection of claims 1 and 4-10 under 35 U.S.C. § 112 (first paragraph) for lack of written descriptive support is rendered moot with respect to claims 1 and 4-10, and is respectfully traversed with respect to new claims 40-51.

For substantially the same reasons as noted above, one of ordinary skill in the art would fully recognize that applicants were in possession of isolated DNA molecules from sources other than *Pseudomonas syringae* pv. *tomato* that encode HrpW homologs. These isolated DNA molecules were present in the individual gel blots to which the *hrpW* probe hybridized. Although applicants did not completely sequence each and every hybridizing nucleic acid, such sequencing is not necessary given the nature of the hybridization conditions (high stringency) and the partial sequencing and restriction mapping, which together demonstrated a high degree of structural homology. From this work applicants have demonstrated that *hrpW* is indeed widespread among Gram negative pathogens and, like other hypersensitive response elicitors, HrpW is characterized by an ability to elicit a

hypersensitive response-like necrosis in non-host plant tissues. Therefore, written descriptive support does indeed exist for the presently claimed invention given the above amendments to specify hybridization and wash conditions.

The burden of establishing that an application lacks adequate written descriptive support falls on the PTO. *See In re Wertheim*, 541 F.2d 257, 263, 191 USPQ 90, 97 (CCPA 1976) ("[T]he PTO has the initial burden of presenting evidence or reasons why persons skilled in the art would not recognize in the disclosure a description of the invention defined by the claims."). According to the Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, ¶1, "Written Description" Requirement, 66 Fed. Reg. 1099 (January 5, 2001), when the genus represents widely variant species more than one species is required, yet when the genus represents closely related species as few as one species may be sufficient. 66 Fed. Reg. at 1106. Thus, size of the genus is clearly of less import than variance of species within the genus. In this case, the *direct* evidence presented in the specification demonstrates that variance is at a minimum given the recited hybridization and wash conditions, the partial sequencing, and restriction mapping. The PTO, on the other hand, has provided no evidence concerning variance within the genus.

For these reasons, the rejection of claims 1 and 4-10 as lacking written descriptive support should be withdrawn, and should not be applied to new claims 40-51.

The rejection of claims 1-10 under 35 U.S.C. § 112 (second paragraph) for indefiniteness is respectfully traversed in view of the above amendments specifying the limitations of the hybridization conditions and the wash conditions. Therefore, this rejection should be withdrawn.

The rejection of claims 6, 7, and 10 under 35 U.S.C. § 112 (second paragraph) for indefiniteness is respectfully traversed in view of the above amendments reciting the presence of a promoter operably coupled to the DNA molecule. Therefore, this rejection should be withdrawn.

The rejection of claims 1 and 4-10 under 35 U.S.C. § 102(a) as being anticipated by Tabakaki et al., "Expression of the *Pseudomonas syringae* pv. *phaseolicola hrpZ* Gene in Transgenic Tobacco and *Saccharomyces cerevisiae*," *In Developments in Plant Pathology: Pseudomonas Syringae Pathovars and Related Pathogens*, Rudolph et al. (eds.), Kluwer Acad. Publ. (Norwell, MA) pp. 392-396 (1997) ("Tabakaki") is respectfully traversed. The PTO cites Tabakaki for the proposition that the *hrpZ* gene would share at least one nucleotide with SEQ ID NO: 1 and its encoded protein would share at least one amino

acid with the protein of SEQ ID NO: 2. Applicants submit that the PTO's position is obviated by the above amendments, because Tabakaki does not teach a DNA molecule as recited in claim 1. Therefore, the rejection of claims 1 and 4-10 should be withdrawn.

Tabakaki likewise does not anticipate claims 40-51. Attached hereto as Exhibit 2 is an alignment between *hrpZ* of *Pseudomonas syringae* pv. *phaseolicola* (obtained from GenBank Accession AF268940) and SEQ ID NO: 1. This alignment shows that homology between the two sequences is extremely low. Therefore, *hrpZ* of *Pseudomonas syringae* pv. *phaseolicola* would not hybridize to the complement of SEQ ID NO: 1 under the recited conditions.

The rejection of claims 1 and 4-10 under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent No. 5,850,015 to Bauer et al. (the "Bauer '015 patent") is respectfully traversed. The PTO cites to the Bauer '015 patent for the proposition that the $hrpN_{Ech}$ gene would share at least one nucleotide with SEQ ID NO: 1 and its encoded protein would share at least one amino acid with the protein of SEQ ID NO: 2. Applicants submit that the PTO's position is obviated by the above amendments, because the Bauer '015 patent does not teach a DNA molecule as recited in claim 1. Therefore, the rejection of claims 1 and 4-10 should be withdrawn.

The Bauer '015 patent likewise does not anticipate claims 40-51. Attached hereto as Exhibit 3 is an alignment between *hrpN* of *Erwinia chrysanthemi* and SEQ ID NO: 1. This alignment shows that homology between the two sequences is extremely low. Therefore, *hrpN* of *Erwinia chrysanthemi* would not hybridize to the complement of SEQ ID NO: 1 under the recited conditions.

The objections to claims 2-5, 7, and 9-10 have been overcome by the above amendments and should be withdrawn.

In view of all of the foregoing, applicants submit that this case is in condition for allowance and such allowance is earnestly solicited.

Respectfully submitted,

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